IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Patent Application of	Conf. No.: 4537
William LEVINE et al	Atty. Ref.: GPK-4110-42
Serial No. 10/536,800	TC/A.U.: 1655
Filed: May 27, 2005	Examiner: CHEN, Catheryne

For: SOLID MUCOADHESIVE COMPOSITION

* *

August 6, 2010

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPEAL BRIEF

Sir:

Appellant hereby **appeals** to the Board of Patent Appeals and Interferences from the last decision of the Examiner.

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(I) REAL PARTY IN INTEREST

The real party in interest is IZUN Pharmaceuticals Corp., a corporation of the state of Delaware.

(II) RELATED APPEALS AND INTERFERENCES

The appellant, the undersigned, and the assignee are not aware of any related appeals, interferences, or judicial proceedings (past or present), which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

(III) STATUS OF CLAIMS

Claims 1-3 and 5-16 are pending and have been rejected. No claims have been substantively allowed. Claim 4 has been canceled.

Applicants appeal the claim rejections of claims 1-3 and 5-16.

(IV) STATUS OF AMENDMENTS

No amendments have been filed since the date of the Final Rejection.

(V) SUMMARY OF CLAIMED SUBJECT MATTER

In this section and throughout the brief, page/column and line numbers are cited in the format of "page/column:line(s)"; for example, a citation to lines 20 to 25 on page 1 of the specification would appear as "(Specification at 1:20-25.)." Moreover, all citations are to PCT/IL2003/000159, published as PCT Pub. No. WO 2004/047816 A1.

The invention of the claims relates to a muco-adhesive solid therapeutic compositions and methods of treating mucosal tissue.

In an aspect, the claims generally relate to a muco-adhesive solid therapeutic composition containing an active ingredient that is a mixture of extracts obtained from the plant species *Sambucus nigra, Centella asiatica* and *Echinacea purpurea*. (*See, e.g.*, Specification at 3:17-21.) The composition includes excipients comprising a bulk ingredient, an adhesive polymer of acrylic acid and polyvinylpyrrolidone; wherein the muco-adhesive solid therapeutic composition adheres to mucosal tissue. (*See, e.g.*, Specification at 3:22-24.)

In another aspect, the claims relate to a muco-adhesive solid therapeutic composition in the form of a tablet, wherein the surface of said tablet is partially coated with a non-adhesive material, such that said tablet is provided with a first, adhesive side and a second, coated, non-adhesive side. (*See, e.g.*, Specification at 3:25-4:8.) In a further aspect, the claims relate to a muco-adhesive solid therapeutic composition includes an active ingredient in an amount from 5 to 15 percent, lactose in an amount from 50 to 65 percent, an adhesive polymer of acrylic acid in an amount from 10 to 20 percent, and polyvinylpyrrolidone in an amount from 10 to 20 percent, or a mixture thereof, based on the total weight of the composition. (*See, e.g.*, Specification at 5:6-13.)

In another aspect, the muco-adhesive solid therapeutic composition according to the invention includes hydroxypropyl cellulose. (*See, e.g.*, Specification at 5:19-22.) In further aspects, the muco-adhesive solid composition is structurally suitable for buccal administration, vaginal administration, or anal administration. (*See, e.g.*, Specification at 8:10-21.)

In yet a further aspect, the claims relate to a method of treating a mucosal tissue in a patient by contacting a mucosal tissue lesion with a therapeutically effective amount of a muco-adhesive solid therapeutic composition containing an active ingredient that is a mixture of extracts obtained from the plant species *Sambucus nigra, Centella asiatica* and *Echinacea purpurea,* and excipients, said excipients comprising a bulk ingredient, an adhesive polymer of acrylic acid and polyvinylpyrrolidone. (*See, e.g.*, Specification at 3:17-24 & 7:17-24.) In an aspect, the method may relate to applying the composition to buccal mucosal tissue, vaginal mucosal tissue, and anal mucosal tissue. (*See, e.g.*, Specification at 8:10-21.) In a further aspect, the composition is provided in the form of a tablet, and wherein a surface of the tablet is partially coated with a non-adhesive material, such that said tablet is provided with a first, adhesive side and a second, coated, non-adhesive side. (*See, e.g.*, Specification at 3:25-4:8.) In yet a further aspect, the method includes contacting the first, adhesive side of the tablet with the mucosal tissue lesion, such that the coated non-adhesive side projects away from said lesion. (*See, e.g.*, Specification at 4:8-14.)

In another aspect, the amount of said *Sambucus nigra* extract ranges between about 0.05 mg to about 15 mg, the amount of said *Centella asiatica* extract ranges between about 0.05 mg to about 15 mg, and the amount of said *Echinacea purpurea*

extract ranges between about 0.05 mg to about 15 mg. (*See, e.g.*, Specification at 7:24-28.) In an aspect, contacting of the composition to a mucosal legion occurs for a period of time ranging between about 1 hour and about 5 hours. (*See, e.g.*, Specification at 8:5-7.)

(VI) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Applicants appeal the rejections of claims 1-3, and 8-16 as allegedly unpatentable as obvious under 35 U.S.C. § 103 over U.S. Patent No. 6,217,908 to Mathiowitz et al. (Mathiowitz); a document retrieved from the internet in 2009 titled "1001herbs"; a document retrieved from the internet in 2009 titled "Holistic-Online"; and Ceschel et al., *Design and Evaluation of Buccal Adhesive Hydrocortisone Acetate (HCA) Tablets*, Drug Delivery 8:161-171 (2001) (Ceschel).[1]

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[1] Although the rejection does not purport to include claims 5-7, Applicants note that the Examiner has not indicated that they would be allowable.

(VII) ARGUMENT

The Examiner rejected claims 1-3 and 8-16 as allegedly unpatentable as obvious under 35 U.S.C. § 103 over U.S. Patent No. 6,217,908 to Mathiowitz et al. (Mathiowitz); a document retrieved from the internet in 2009 titled "1001herbs"; a document retrieved from the internet in 2009 titled "Holistic-Online"; and Ceschel et al., *Design and Evaluation of Buccal Adhesive Hydrocortisone Acetate (HCA) Tablets*, Drug Delivery 8:161-171 (2001) (Ceschel). Applicants understand that the rejection was likely intended to also apply to claims 5-7.

Applicants assert that all claims are patentable over the asserted prior art. Applicants, however, argue the patentability of certain dependent claims separately, as these claims raise further issues with the rejection. No single claim is representative of the inventive subject matter defined by the pending claims.

A. The Internet Publications From 2009 Are Not Prior Art

Applicants note the two internet "publications" bear a retrieval dates well after the priority (and filing) date of this application. According to MPEP § 2128 (with emphasis added): "Prior art disclosures on the Internet or on an on-line database are considered to be publicly available as of the date the item was publicly posted. Absent evidence of the date that the disclosure was publicly posted, if the publication itself does not include a publication date (or retrieval date), it cannot be relied upon as prior art under 35 U.S.C. 102(a) or (b)." Accordingly, the Patent Office has not demonstrated that these documents retrieved from the internet in 2009 were indeed publicly available prior art prior to retrieval in 2009.

Moreover, merely posting a copyright notice is insufficient to show the precise *content*, if any, of the pages at any time prior to the retrieval date. *Cf. Paris Glove of Canada Ltd. v. SBC/Sporto Corp.*, 84 USPQ2d 1856, 1858-59 (TTAB 2007) (holding that even material obtained from the "Wayback Machine" is unreliable).

In response, the Examiner summarily concludes that 1001herbs "can go back to an internet date of 1998" and cites a webpage also retrieved in 2009 in support of that position. (Final Office Action at 7.)

First, the Examiner has made no attempt to show that Holistic-Online was available before the effective filing date of the present application. Thus, it appears that the Examiner agrees that Holistic-Online is not prior art. Indeed, the Examiner only attempted to demonstrate that 1001herbs was prior art. There is no similar evidence of record for Holistic-Online.

Second, the Examiner seeks to use a webpage dated 2009 to show the date of another webpage 2009. Specifically with respect to the "Internet Archive" cited for 1001herbs, the TTAB has reasonably explained that "the database itself is not self-authenticating and there is no reason to treat its existence as authenticating the pages in its historical record." *Paris Glove*, 84 USPQ2d at 1858. Thus, there is insufficient evidence to show that the website dated 2009 is an authentic representation of what the cited reference may have looked like prior to the effective filing date of the present invention. For example, the purported "prior art" version shows differences from the 2009 version cited in the Final Office Action (e.g., stating that the "Elderberry Combo contains 450 mg per capsule of Elderberry extract, *Echinacea purpurea*, and Royal jelly" versus stating "[e]ach Elderberry Defense capsule contains 394 mg of elderberry extract,

Echinacea purpurea, and royal jelly"). It is unclear whether Elderberry Defense is the same as Elderberry Combo, and how they differ.

Even assuming, for the sake of argument, that the cited internet publications are "prior art," they do not render the pending claimed subject matter unpatentable, either alone or in combination with the other cited references.

B. The Claims Would Not Have Been Obvious

Claims 1 & 11:

As defined in the pending claims, the invention relates to a therapeutic composition having the following features:

(1) The active ingredient is a mixture comprising extracts of three specific herbs (extracts of the plants *Sambucus nigra, Centella asiatica* and *Echinacea purpurea*).

(2) The composition is in a solid form and is mucoadhesive, and therefore adheres to the mucosal tissue (in order to locally treat inflamed mucosa).

(3) The composition contains excipients: an adhesive polymer of acrylic acid, polyvinylpyrrolidone and also a bulk ingredient (lactose).

An important aspect of the presently claimed subject matter is that a mixture of extracts obtained from the plants *Sambucus nigra, Centella asiatica* and *Echinacea purpurea* is incorporated in a solid mucoadhesive composition together with a polymer of acrylic acid and polyvinylpyrrolidone, with the benefit of attaining a dosage form having enhanced bioadhesiveness. The improved bioadhesiveness unexpectedly attained by the solid composition of the invention is illustrated in the working examples in the specification. The experimental results given in the description indicate a considerable increase in the adhesiveness of the composition, following the addition of the three herbs

mixture. (*See, e.g.*, Specification at 10-14.) The mucoadhesive composition of the claimed invention may therefore be placed onto the mucosa, to effectively deliver the herbs and accomplish the local treatment. It is noted that the mixture of herbs constitutes the active ingredient to be delivered by solid dosage form and to be absorbed by the mucosa, and at the same time, the herbal mixture contributes appreciably to the overall adhesiveness of the solid dosage form.

Subject matter is unpatentable as obvious only "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a). When determining whether a claimed combination of known elements would have been obvious, the statutory inquiry is guided by "whether the improvement is more than the predictable use of prior art elements according to their established functions." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007). This inquiry is factual in nature. *Cf. Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165 (Fed. Cir. 2006) (explaining that whether there is "a reasonable expectation of success in making the invention via" a combination of prior art elements is a question of fact). Answering this question usually entails considering the "interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue." *KSR*, 550 U.S. at 418. What a reference teaches, whether there is a trend or demand in the relevant marketplace or design community, the

background knowledge of one of skill in the art—these are all questions reserved for the finder of fact. *See Digital Control, Inc. v. Charles Mach. Works*, 437 F.3d 1309, 1316 (Fed. Cir. 2006) ("[W]hat a reference teaches is a question of fact . . . .").

An obviousness analysis "may include recourse to logic, judgment, and common sense available to the person of ordinary skill that do not necessarily require explication in any reference or expert opinion." *Perfect Web Technologies, Inc. v. InfoUSA, Inc.*, 587 F.3d 1324, 1329 (Fed. Cir. 2009). Nevertheless, "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006). As recently held by the Federal Circuit, "[m]erely saying that an invention is a logical, commonsense solution to a known problem does not make it so." *TriMed, Inc. v. Stryker Corp.*, ___ F.3d ___, No. 2009-1423, slip op. at 15 (June 9, 2010) (emphasis added). Accordingly, there must be substantial evidence in the record to support the rejection; speculation is insufficient.[2]

The Final Office Action primarily relies on Mathiowitz.

Mathiowitz is concerned with the enhancement of the bioadhesiveness of polymeric microcapsules. To this end, the patent suggests the modification of the microcapsules through the covalent binding of lectin onto their surface. At the outset it should be pointed out that Mathiowitz contains no disclosure of *Centella* or *Echinacea* and certainly no disclosure of a mixture comprising the three herbs as employed according to the present invention: "[Mathiowitz] does not teach *Echinacea purpurea*, *Centella asiatica*, lactose, contact time." (Final Office Action at 3.) Furthermore, it is

[2] Applicants note that the previous rejections of the claims over very similar teachings of different references were overcome.

respectfully submitted that Mathiowitz also does not teach the combination of an adhesive polymer of acrylic acid, polyvinylpyrrolidone and *Sambucus nigra*.

Regarding the polymers which can be used for making the microcapsules, it is noted that Mathiowitz provides a large list of suitable polymers on column 7 and 8. Although polyacrylic acid and polyvinylpyrrolidone are mentioned in the list, there is no enabled disclosure of a combination comprising both these polymers, and Mathiowitz's working examples clearly give preference to *other* types of polymers. *Cf. In re Arkley*, 455 F.2d 586, 587 (CCPA 1972) ("[T]he [prior art] reference must clearly and unequivocally disclose the claimed [invention] or direct those skilled in the art to the [invention] without any need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference.")

Regarding the *Sambucus nigra*, Mathiowitz only briefly mentions said herb as a possible source of lectin. In Column 11 of the patent, a large list of sources for lectin is provided, one of which is identified *Sambucus nigra*. More specifically, the language of the paragraph is as follows (emphasis added):

> Lectins that can be covalently attached to microspheres to render them target specific to the mucin and mucosal cell layer could be used as bioadhesives. Useful lectin ligands include lectins isolated from: *Abrus precatroius, Agaricus bisporus, Anguilla anguilla, Arachis hypogaea, Pandeiraea simplicifolia, Bauhinia purpurea, Caragan arobrescens, Cicer arietinum, Codium fragile, Datura stramonium, Dolichos biflorus, Erythrina corallodendron, Erythrina cristagalli, Euonymus europaeus, Glycine max, Helix aspersa, Helix pomatia, Lathyrus odoratus, Lens culinaris, Limulus polyphemus, Lysopersicon esculentum, Maclura pomifera, Momordica charantia, Mycoplasma gallisepticum, Naja mocambique,* as well as the lectins *Concanavalin A, Succinyl-Concanavalin A, Triticum vulgaris, Ulex europaeus I, II* and *III, Sambucus nigra, Maackia amurensis, Limax*

fluvus, Homarus americanus, Cancer antennarius, and *Lotus tetragonolobus.*

Of note, there is no teaching in Mathiowitz that the lectins from *Sambucus nigra* are to be preferred over any of the other lectins mentioned in the list. Furthermore, to be useful the lectins (which are carbohydrate-binding proteins and in the case of *Sambucus* are found only in extracts of the bark of the tree) would need to be covalently linked to the microsphere surface disclosed in Mathiowitz. It follows that the *Sambucus nigra* lectin incorporated in the composition of Mathiowitz is necessarily in a covalently bound form.

The *Sambucus nigra* lectin is not an active ingredient to be delivered by the composition of Mathiowitz. Instead the reference provides a separate list of active materials that can be incorporated into the composition (see column 14). Moreover, there is no indication in Mathiowitz that the microspheres are suitable for delivering plant materials. All a person of ordinary skill in the art would glean from Mathiowitz is that if *Sambucus nigra* lectin is to be used, then it needs to be covalently linked to the polymeric microsphere.

To summarize some of the deficiencies of Mathiowitz: the total number of possible combinations of polymers and lectin sources disclosed is undoubtedly a very large number; the reference gives no preference to making microcapsules made of polyacrylic acid and polyvinylpyrrolidone combined with *Sambucus nigra* lectin. Even if there were an express suggestion in Mathiowitz to combine *Sambucus nigra* lectin with these two particular polymers, the combination would still require some chemical modification in order to allow the covalent binding between the chemical species. It is

not at all clear how polyacrylic acid and polyvinylpyrrolidone can be combined to form a mixed microcapsule, and how the covalent binding of the *Sambucus nigra* lectin to the polyvinylpyrrolidone would alter the chemical structure of the latter. It is absolutely clear, however, that a non-covalent association of *Sambucus nigra* lectin with the microspheres is not taught by Mathiowitz. According to the presently claimed subject matter, the plant extracts are active ingredients and are, therefore, incorporated in a non-covalently bound form.

In order to supplement the deficiencies of Mathiowitz, the Examiner relies on several secondary prior art references: "1001 herbs" (dated 2009) and "Holistic-Online" (dated 2009) and Ceschel.

Applicants point out that that "1001 Herbs" and "Holistic-Online" merely and summarily mention the medicinal properties of certain combination of herbs. In order to justify the combination of the three herbs with the drug delivery system of Mathiowitz, the Patent Office appears to the take the position that the mere possibility that the extant herbs can be combined is enough to show that a person of ordinary skill in the art would have found it obvious to have combined them:

> The drug delivery of Mathiowitz et al. can be used to deliver the 1001herbs taught *Echinacea purpurea* and elderberry or *Sambucus nigra* at 394 mg for use in boosting immune system (paragraph 1) and Holistic-online taught *Centella asiatica* or *gotu kola* for treating fever, immune system strengthening (page 2, Useful for) and infections (page 2, paragraph 2) Thus, an artisan of ordinary skill would reasonably expect that ingredients that can boost immune system could be used as the type composition for delivery taught by the references. This reasonable expectation of success would motivate the artisan to use *Sambucus nigra*, *Centella asiatica* and *Echinacea purpurea* as the muco-adhesive drug in the reference composition. Thus, using *Sambucus nigra*, *Centella asiatica* and

> *Echinacea purpurea* as the mucoadhesive drug is considered an obvious modification of the references.

(Final Office Action at 5-6 (emphasis added).)

However, the medicinal properties of *Echinacea purpurea and Centella asiatica* reported separately in "1001 Herbs" and "Holistic online," respectively, are completely unrelated to the formulation of the three herbs in a solid dosage form exhibiting enhanced mucoadhesion. The question to be considered is whether the primary reference and secondary references fairly provide the reader with sufficient information to encourage a formulation comprising *Echinacea purpurea, Centella asiatica* and *Sambucus nigra* together with a polymer of acrylic acid and polyvinylpyrrolidone, to provide a mucoadhesive dosage form, with an expectation that a greater adhesion is attained by the addition of said herbs.

The references cited are silent regarding the delivery of *Echinacea purpurea and Centella asiatica* in a mucoadhesive composition and their capacity to increase the adhesiveness of a solid dosage form. The fact that the herbs possess therapeutic properties pertinent to various ailments in no way suggests that they would enhance adhesion to mucosal surfaces. Thus, there is absolutely no prior teaching based on the medicinal properties of *Echinacea* and *Centella* described in the references cited that would lead one to expect that the combination of *Sambucus*, *Centella*, and *Echinacea*, when added to adhesive polymers, (polymer of acrylic acid, polyvinylpyrrolidone), enhances adhesion of the resulting composition, to afford a solid dosage form which is mucoadhesive.

Merely finding the preexisting herbs in purportedly prior art references then asserting that they "can" be combined in accordance with the claims is simply insufficient to conclude that the claimed subject matter would have been obvious. It is apparent that the Final Office Action places its exclusive rationale on each reference teaching that the relevant *Sambucus*, *Centella*, and *Echinacea*, "boosting immune system." (*See* Final Office Action at 5.)

This rationale finds no support in the evidence. First, Mathiowitz does not disclose any effects of *Sambucus* on the immune system. Again, *Sambucus* is merely mentioned in a laundry list of possible sources for lectin ligands. Second, "herbs1001" merely states that "*Echinacea* is the most popular herb in America for the immune system; it is mild and suitable for all ages." There is no disclosure or teaching that it "boosts" the immune system, and the Examiner has provided no evidence that being mild and suitable for all ages means that the herb boosts the immune system. And third, "Holistic-Online" teaches that *Centella* can be useful for "immune system strengthening (cleansing and nourishing)" as well as AIDS, Epilepsy, Eczema, Vericose veins, venereal diseases, among other things. To the extent that it may mention "boosting immune system," that is undermined by the outlandish claims that the herb is useful in treating ailments as disparate as AIDS and eczema. Regardless, it remains clear that not all three references teach using the three herbs in the same way (i.e., "boosting the immune system").

Regarding the combination of Mathiowitz with Ceschel, the Final Office Action appears to take the position:

> Ceschel et al. teaches mucoadhesive, specifically buccal, administration likes lozenges, troches, gels, oral rinse or mouthwash for delivery of drugs through the mucosa of the oral cavity (page 161, paragraph 2) and composition for tablets with lactose at amounts of 42.1 7, 37.1 7, 32.1 7%, mucoadhesive PVP (polyvinylpyrrolidone) PK30 at amounts of 10, 20, 30% (page 162, Table 1) with Table 8 showing tablet detachment or disgregation time at 1 hour 24 minutes. Thus, it would be obvious to add lactose into mucoadhesive formulation, such as that taught by Ceschel et al. An artisan of ordinary skill would clearly expect that the bioadhesive tablets taught by Ceschel et al. would function successfully to administer the bioadhesive microcapsules taught by Mathiowtiz et al. This reasonable expectation of success would motivate the artisan to modify Mathiowtiz et al. to include lactose as an effective means to administer the bioadhesive formulation.

(Final Office Action at 6 (emphasis added).)

Applicants respectfully disagree. It should be pointed out that Mathiowitz is concerned with polymeric microspheres. And column 14, lines 43-48, explains that the microspheres are administered in suspension or in ointment to the mucosal membranes. Thus, the microspheres of Mathiowitz are not intended to be used to form a tablet. There is no indication that the microspheres can be processed to form tablets (e.g., that the microspheres are flowable; that the microspheres can be wet granulated and compressed).

Because the independent claims (i.e., claims 1 and 11) are patentable, the dependent claims are also patentable. *See In re Fine*, 837 F.2d 1071, 1076 (Fed. Cir. 1988). Nevertheless, Applicants point out that the dependent claims have further features that buttress their independent patentability.

Claims 2 & 13 The Final Office Action did not provide any reasoning why the structure of claims 2 and 13, which are directed to a tablet having specific structure (adhesive face and a coated, non-adhesive face) is "intrinsically taught" – that is, necessarily present – in Mathiowitz. At best, the Final Office Action states: "Mathiowitz

et al. teaches bioadhesive polymers in the form of or as a coating on microcapsules containing drugs or bioactive substance (column 3, lines 56-57). The coated side will [be] the adhesive, while the non-coated side will be the non-adhesive side. The inside of the shell would be in contact with the dispersing agent; thus, the dispersing agent would be the non-adhesive side." (Final Office Action at 10.)

But this citation to Mathiowitz does not show that the claimed structure is "intrinsically taught." Inherency, of course, requires certainty, not possibility. *See In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) ("To establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.").

Furthermore, the Examiner misunderstands the subject matter recited in claims 2 and 13. These claims recite a tablet having an adhesive face and a coated, non-adhesive face. The Examiner finds the "intrinsic teaching" of Mathiowitz to be the reverse: that the coated side is adhesive, and the non-coated side is non-adhesive. Accordingly, the rejection of claims 2 and 13 should be reversed.

Claim 14: Claim 14 further recites contacting the first, adhesive side of the tablet with the mucosal tissue lesion, such that the coated non-adhesive side projects away from said lesion. Again, the Examiner appears to cite the bioadhesive polymer of Mathiowitz as contacting the lesion.

Claim 3: Claim 3 recites a muco-adhesive solid therapeutic composition according to claim 1, comprising the active ingredient in an amount from 5 to 15 percent, lactose in an amount from 50 to 65 percent, an adhesive polymer of acrylic acid in an amount from

10 to 20 percent, and polyvinylpyrrolidone in an amount from 10 to 20 percent, or a mixture thereof, based on the total weight of the composition. The Final Office Action admits that "The references do not specifically teach adding the ingredients in the amounts claimed by applicant." (Final Office Action at 6.) But without citing any evidence in support, the Examiner nakedly asserts that with respect to the particularly recited weight percentages for each ingredient: "The amount of a specific ingredient in a composition that is used for a particular purpose (the composition itself or that particular ingredient) is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize." (Final Office Action at 6.) Merely stating something is a result-effective variable does not make it so – evidence is required.

The Final Office Action cites no evidence that (1) the amount of active ingredient comprising *Sambucus*, *Centella*, and *Echinacea*, (2) the amount of lactose, (3) the amount of an adhesive polymer of acrylic acid, and (4) the amount of polyvinylpyrrolidone would all four together be optimized in the amounts recited in claim 3. This is especially true, because the Final Office Action does not assert that these four components were known in a single reference. Thus, the Examiner is not merely optimizing a known set of variables; rather, the Examiner is first selecting, choosing, and combining extant elements, then asserting it would have been obvious to optimize the combination. This is too far removed from the teachings of the individual references. Accordingly, claim 3 is not unpatentable.

Claim 15: Claim 15 further defines the method of claim 13, specifically reciting that the amount of said *Sambucus nigra* extract ranges between about 0.05 mg to about 15 mg, the amount of said *Centella asiatica* extract ranges between about 0.05 mg to

about 15 mg, and the amount of said *Echinacea purpurea* extract ranges between about 0.05 mg to about 15 mg. Like with respect to claim 3, the Final Office Action makes no effort to explain why these are result-effective variables. Indeed, there is nothing in Mathowitz to show that *Sambucus* has any beneficial properties with respect to boosting the immune system as required by the rationale expressed in the Final Office Action.

Again, the Examiner is not merely optimizing a known set of variables; rather, the Examiner is first combining extant herbs, then asserting it would have been obvious to optimize the combination. Accordingly, claim 15 is not unpatentable.

CONCLUSION

In conclusion it is believed that the application is in clear condition for allowance; therefore, early reversal of the Final Rejection and passage of the subject application to issue are earnestly solicited.

Respectfully submitted,

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(VIII) CLAIMS APPENDIX

1. (Previously Presented) A muco-adhesive solid therapeutic composition containing an active ingredient that is a mixture of extracts obtained from the plant species *Sambucus nigra, Centella asiatica* and *Echinacea purpurea,* and excipients, said excipients comprising a bulk ingredient, an adhesive polymer of acrylic acid and polyvinylpyrrolidone; wherein the muco-adhesive solid therapeutic composition adheres to mucosal tissue.

2. (Previously Presented) A muco-adhesive solid therapeutic composition according to claim 1 provided in the form of a tablet, wherein the surface of said tablet is partially coated with a non-adhesive material, such that said tablet is provided with a first, adhesive side and a second, coated, non-adhesive side.

3. (Previously Presented) A muco-adhesive solid therapeutic composition according to claim 1, comprising the active ingredient in an amount from 5 to 15 percent, lactose in an amount from 50 to 65 percent, an adhesive polymer of acrylic acid in an amount from 10 to 20 percent, and polyvinylpyrrolidone in an amount from 10 to 20 percent, or a mixture thereof, based on the total weight of the composition.

4. (Canceled)

5. (Previously Presented) A muco-adhesive solid therapeutic composition according to claim 1 further comprising hydroxypropyl cellulose.

6. (Previously Presented) A muco-adhesive solid therapeutic composition according to claim 2 further comprising hydroxypropyl cellulose.

7. (Previously Presented) A muco-adhesive solid therapeutic composition according to claim 3 further comprising hydroxypropyl cellulose.

8. (Previously Presented) A muco-adhesive solid composition according to claim 1, wherein the muco-adhesive solid composition is structurally suitable for buccal administration.

9. (Previously Presented) A muco-adhesive solid composition according to claim 1, wherein the muco-adhesive solid composition is structurally suitable for vaginal administration.

10. (Previously Presented) A muco-adhesive solid composition according to claim 1, wherein the muco-adhesive solid composition is structurally suitable for anal administration.

11. (Previously Presented) A method of treating a mucosal tissue in a patient comprising the step of: contacting a mucosal tissue lesion with a therapeutically effective amount of a muco-adhesive solid therapeutic composition containing an active ingredient that is a mixture of extracts obtained from the plant species *Sambucus nigra, Centella asiatica* and *Echinacea purpurea,* and excipients, said excipients comprising a bulk ingredient, an adhesive polymer of acrylic acid and polyvinylpyrrolidone.

12. (Previously Presented) A method according to claim 11, wherein said mucosal tissue is selected from the group consisting of buccal mucosal tissue, vaginal mucosal tissue, and anal mucosal tissue.

13. (Previously Presented) A method according to claim 11, wherein said muco-adhesive composition is provided in the form of a tablet, and wherein a surface of the tablet is partially coated with a non-adhesive material, such that said tablet is provided with a first, adhesive side and a second, coated, non-adhesive side.

14. (Previously Presented) A method according to claim 13 comprising contacting the first, adhesive side of the tablet with the mucosal tissue lesion, such that the coated non-adhesive side projects away from said lesion.

15. (Previously Presented) A method according to claim 13, wherein an amount of said *Sambucus nigra* extract ranges between about 0.05 mg to about 15 mg, wherein an amount of said *Centella asiatica* extract ranges between about 0.05 mg to about 15 mg, and wherein an amount of said *Echinacea purpurea* extract ranges between about 0.05 mg to about 15 mg.

16. (Previously Presented) A method according to claim 11, wherein the step of contacting occurs for a period of time ranging between about 1 hour and about 5 hours.

(IX) EVIDENCE APPENDIX

(None.)

(X) RELATED PROCEEDINGS APPENDIX

(None.)